



Anticholinergic Drug Use in Dementia Patients

Introduction:

Elderly dementia patients are at increased risk to experience both polypharmacy and comorbidities more than other age groups. This vulnerable population also tends to tolerate drugs less favorably than healthy older adults. One of the main reasons for this increased sensitivity to the adverse effects of medications is the physiological nature of the aging body (i.e. decreased renal function, etc.). In addition, these patients are less able or likely to detect or report a side effect from their medications and caregivers may not be able to delineate side effects from the normal aging process.

With all these obstacles in mind, prescribers are responsible to prevent, detect and mitigate these issues through careful clinical decision-making when prescribing for elderly dementia patients. It is also important for prescribers to consider that there are many drug classes that possess **strong anticholinergic properties. They are also reported by the American Geriatric Society in the Updated Beers Criteria (2012) as Potentially Inappropriate Medications (PIMs) for the elderly and should be avoided.** Anticholinergic drugs act by binding reversibly to muscarinic cholinergic receptors and compete with acetylcholine. The National Committee for Quality Assurance (NCQA) has noted that one study found that 32% of patients 65 or older who visit an emergency department were taking at least one potentially inappropriate medication. In addition, a study published in the June 24, 2011 Journal of the American Geriatric Society reported that medications with anticholinergic activity increase the cumulative risk of cognitive impairment and death. The study included over 13,000 men and women aged 65 and older. Researchers found that 47% of participants reported taking medications with anticholinergic properties (e.g. muscle relaxants, antihistamines, antiemetics, tricyclic antidepressants, and antispasmodics, etc.). The use of medications with definite anticholinergic effects was associated with a 0.33 point greater decline in the Mini-Mental State Examination (MME) than those patients not taking anticholinergics. In addition, two year mortality was greater for those taking definite and possible anticholinergics.

Some medications are intentionally selected for their anticholinergic properties. For example, Ditropan[®] (oxybutynin) is often used for urinary incontinence. The anticholinergic properties interfere with hyperactive detrusor muscles to alleviate incontinence. Unfortunately, none of the currently available products in this class selectively target the M2 or M3 muscarinic receptors of the bladder. As a result, patients may experience a laundry list of potential anticholinergic related side effects such as dry mouth, blurred vision, dizziness, urinary retention, confusion, disorientation, agitation, etc. Lastly, to complicate matters even further, many of these drugs' side effects may be difficult to delineate from the normal aging process.

Drug interactions:

Drug-drug interactions with anticholinergics can present still another important hazard to consider for the elderly patient with dementia. For example, cholinesterase Inhibitors like Aricept[®] (donepezil), Exelon[®] (rivastigmine) and Razadyne[®] (galantamine) were developed to treat Alzheimer's dementia and to slow the progression of loss of cognitive function. These medications have shown to modestly improve cognition in 30%-40% of patients in clinical trials by inhibiting the acetyl cholinesterase enzyme.

Anticholinergics and Cholinesterase inhibitors should not be used concomitantly because they have opposing mechanisms of action. Therefore this drug-drug interaction has the potential to decrease the effectiveness of cholinesterase inhibitors which again may be disguised as an expected decline over time in the patient's condition.

Key points to remember:

- Anticholinergic and sedative medications are known to commonly impair physical and cognitive function with adverse effects ranging from mild cognitive impairment to delirium. These adverse effects can be more profound in older patients with dementia.
- Due to the progressive nature of the disease condition it can be easy to misinterpret the signs of drug induced impairment or adverse effects.
- The old adage of 'go low, go slow' is clearly applicable to the use of anticholinergic medications in the elderly dementia patient population. When therapy with these agents cannot be avoided, prescribers should be careful to consult the FDA labeling or other reliable sources (including your friendly clinical pharmacist!) to determine an appropriate initial dose and schedule. Therapies that don't appear to provide a positive benefit to the patient after an initial trial period should be discontinued.
- **Lastly, while we are on the topic of medications and elderly patients with dementia don't forget that antipsychotics, both 1st and 2nd generation carry an increased risk for CVA (stroke) and mortality in dementia patients.** These should also be avoided in this patient population unless other non-pharmacological/pharmacological therapies have failed to control the patient's symptoms or the patient poses a significant threat to themselves or to others.

References:

1. AGS 2012 Beers Criteria Update Expert Panel. AGS Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. JAGS 2012; 60:60:616-31. Available at www.americangeriatrics.org
2. Bell JS, Mezrani C, Blacker N, LeBlanc T, Frank O, Alderman CO, Rossi S, Rowett D, Shute R. Anticholinergic and sedative medicines- prescribing considerations for people with dementia. Aust Fam Physician. 2012 Jan-Feb; 41 (1-2): 45-9.
3. Effectiveness of anticholinergic drugs compared with placebo in the treatment of overactive bladder: systematic review. BMJ 2003 19; 326:841-4.
4. Facts and Comparisons [internet]. [Cited 2012, June 26]. Available from: <http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-ce10&book=CE>
5. National Committee for Quality Assurance (NCQA). HEDIS R 2011: Healthcare Effectiveness Data and Information Set. Vol. 1, narrative. Washington (DC): National Committee for Quality Assurance (NCQA); 2010. various p.
6. National Committee for Quality Assurance (NCQA). HEDIS R 2011: Healthcare Effectiveness Data and Information Set. Vol. 2, technical specifications. Washington (DC): National Committee for Quality Assurance (NCQA); 2010. various p.
7. Pharmacotherapy choices for patients with dementia. Pharmacist's Letter/Prescriber's Letter 2008; 24(5): 240510.